

## ON THE ELECTROREDUCTION MECHANISM OF $\alpha$ -HALOKETONES

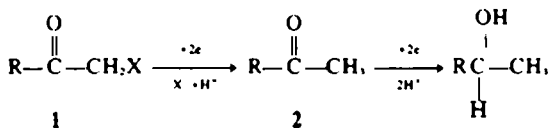
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**Abstract**—The electrolytic reduction of phenacyl chloride 3, phenacyl bromide 4, 4-(chloroacetyl)pyridine 6 and 4-(bromoacetyl)pyridine 7 was investigated and compared to that of the analogous ketones [acetophenone 5 and acetylpyridine 8] and halides [(2-chloroethyl)benzene 9 and (2-bromoethyl)benzene 10]. Current-potential curves on mercury were measured and the products from preparative electrolyses were isolated and identified. The  $\alpha$ -haloketones exhibited two reduction waves, the less negative of which corresponded to the cleavage of the C-X bond while the other was due to the reduction of the resulting ketone. The  $\alpha$ -haloketones in general were found to be more reactive than the analogous halides and this effect was even more pronounced in the pyridine derivatives. A mechanism involving addition of an electron to an orbital delocalized over the carbonyl and the halogen is suggested, to account for this phenomenon.

The electrochemical reduction of  $\alpha$ -haloketones has received considerable attention.<sup>1-13</sup> Polarograms of these compounds show two waves. The  $E_{1/2}$  of the second wave corresponds to that of the analogous ketone and controlled potential electrolysis at the first wave confirmed the following scheme.

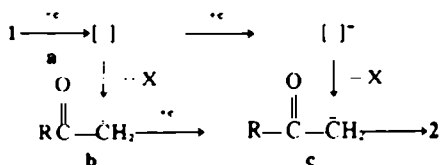


Scheme 1.

It was indicated that the ketone functionality made the potential for halide cleavage (1→2) much less negative than that for alkyl halides. Two mechanisms have been postulated to account for this phenomenon.

(a) The reduction of the halide was regarded as a nucleophilic displacement,<sup>3-6,14</sup> the electrode acting as the nucleophile. The ease of reduction was attributed to the polar effect of the oxygen.

(b) A more widely accepted<sup>11,12,14</sup> reaction pathway would involve discreet electron transfer steps. Assuming no adsorbed intermediates and no acid catalysis, this can be envisaged as follows:



Scheme 2.

It is generally agreed that the first step involves electron transfer and the last is protonation of the enolate anion. Although the timing of the other steps is not resolved, most speculation has centered upon a mechanism involving carbon-halogen bond cleavage in the rate (potential) determining step. Indeed, it has been suggested that the first intermediate is the enolate radical b. But, an

alternative direct 2 electron addition to a has not been disproved.

In the present study an attempt was made to clarify the mechanism of electroreduction of  $\alpha$ -haloketones by investigating the influence of a heteroatom in the parent molecule on the reduction potential.

### RESULTS

The electrochemical behavior of the compounds 3-10 was investigated. Current-potential curves, on a dropping mercury electrode of constant area, in the range of 0 to -2.0 V were recorded.

The curves for several concentrations of 4 are shown in Fig. 1. The  $\alpha$ -haloketones 3, 4, 6 and 7 exhibited two reduction waves while the ketones 5 and 8 had only one wave (Figs. 2 and 3). The normal halides 9 and 10 did not display any reduction wave in the potential range under investigation. Values of  $E_{1/2}$  ( $i = 5\% i_d$ ) were derived from current-potential plots and are shown in the table.

Current-time curves on free falling drops at a constant potential  $E_{1/2}$  (for each compound) were recorded for 3, 4 and 6 and the curves for 3 are shown in Fig. 4. Similar measurements with 7 would have been meaningless as it has an oxidation wave (possibly due to catalytic oxidation of mercury) in the potential range of its  $E_{1/2}$  (Fig. 3).

Preparative constant-potential electrolyses yielded exclusively acetophenone 5 from the benzene derivatives 3 and 4 and 4-acetylpyridine 8 from the pyridine derivatives 6 and 7.

### DISCUSSION

The more positive reduction wave of the  $\alpha$ -haloketones 3, 4, 6 and 7 (Figs. 2 and 3) arises from the cleavage of the carbon-halogen bond as proved by the product analysis. The second is due to the reduction of the ketone formed in the first step as deduced from the coincidence of the  $E_{1/2}$  for acetophenone 5 with  $E_{1/2}$  for the second wave of 3 and 4 (Fig. 2) and in the same manner  $E_{1/2}$  for 4-acetylpyridine 8 and that for 6 and 7 (Fig. 3).

Although the half wave potentials within the benzene and the pyridine series are comparable, the diffusion currents (2nd wave) of the halides are distinctly lower than those of the corresponding ketones (Figs. 2 and 3). Similar phenomena have been observed<sup>15,16</sup> and explained by the different nature (orientation towards the surface,

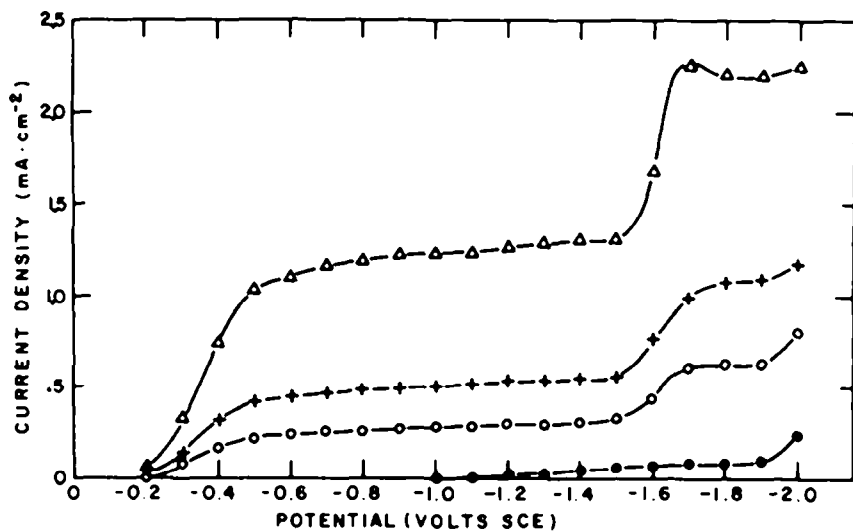


Fig. 1. Current-potential plots for the reduction of phenacyl bromide 4. 0.5 M Et<sub>3</sub>N-*p*-Ts in CH<sub>3</sub>CN:H<sub>2</sub>O (6:1). ● background (b.g.); ○ 1 × 10<sup>-3</sup> M; + 2 × 10<sup>-3</sup> M; △ 5 × 10<sup>-3</sup> M.

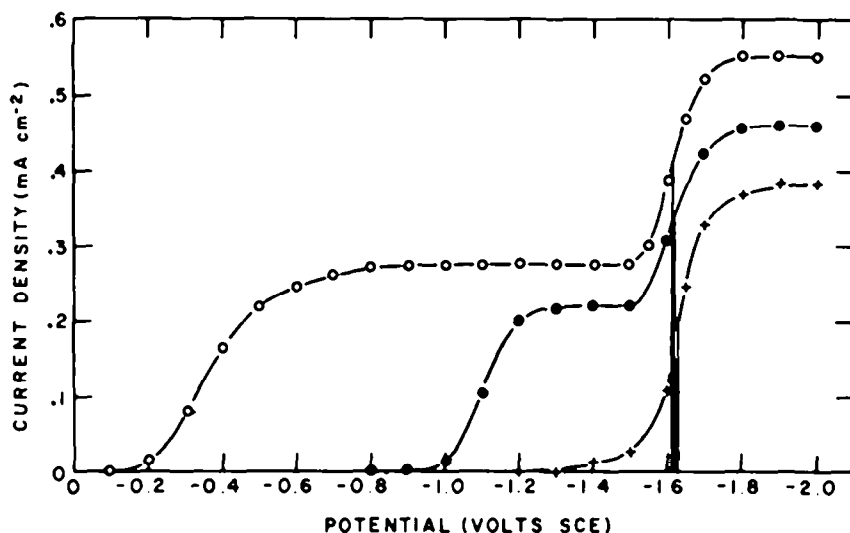


Fig. 2. Current-potential plots for comparison of  $E_{1/2}$  of the benzene derivatives (corrected for b.g.). 1 × 10<sup>-3</sup> M reactant and 0.5 M Et<sub>3</sub>N-*p*-Ts in CH<sub>3</sub>CN:H<sub>2</sub>O (6:1) - acetophenone 5; ● phenacyl chloride 3; ○ phenacyl bromide 4.

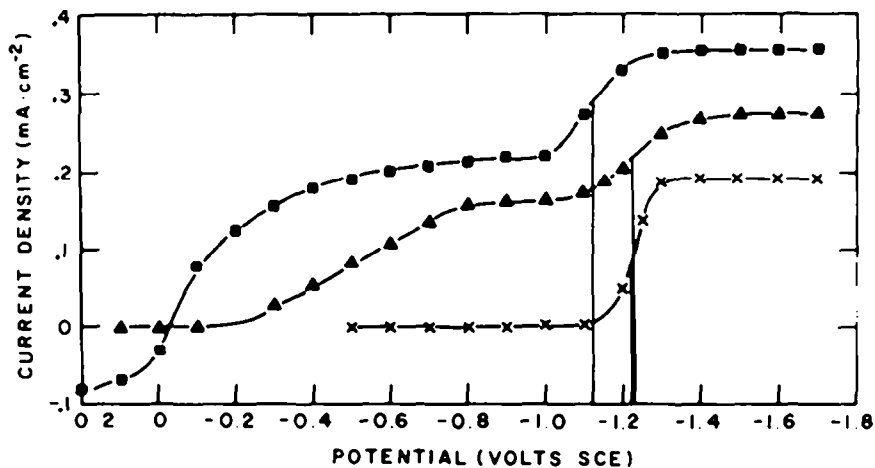


Fig. 3. Current-potential plots for comparison of  $E_{1/2}$  of the pyridine derivatives (corrected for b.g.). 0.5 M reactant and 0.5 M Et<sub>3</sub>N-*p*-Ts in CH<sub>3</sub>CN:H<sub>2</sub>O (6:1), pH 3.0. × acetyl pyridine 8; ▲ 4-(chloroacetyl)pyridine 6; ■ 4-(bromoacetyl)pyridine 7.

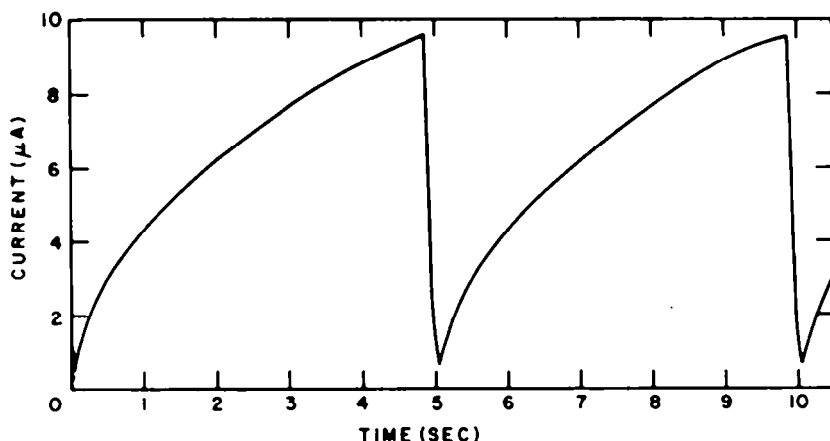


Fig. 4. Current-time plot (corrected for b.g.) for  $5 \times 10^{-3}$  M phenacyl chloride 3 at  $-1.0$  V (SCE).  $0.5$  M  $\text{Et}_4\text{N-p-Ts}$  in  $\text{CH}_3\text{CH}_2:\text{H}_2\text{O}$  (6:1), pH 3.0.

hydration state, etc.) of a species diffusing towards the electrode from the bulk of the solution as opposed to the same species formed *in situ* on the electrode surface.

Comparison between  $\alpha$ -haloketones 3, 4, 6 and 7 and the analogous normal halides 9 and 10 showed that the presence of a carbonyl function in the molecule enhances the ease of cleavage of the C-X bond. The halides 9 and 10 did not reduce at all in the potential range applied, while the  $\alpha$ -haloketones had a wave at even less negative potentials than required for the reduction of the corresponding ketone (Figs. 2 and 3). To understand the nature of the carbonyl influence, we wanted to compare the relative reactivities of the different haloketones by means of their  $E_{1,p}$ † values (eqn 1).<sup>17</sup>

$$E_{1,p} = E^\circ + \frac{2.3 RT}{nF} \log(p-1) 0.886 k_2^{\ddagger} \sqrt{\frac{t}{D}} \quad (1)$$

We treated the bromides and chlorides separately assuming that reaction mechanism and  $E^\circ$  values are the same for compounds within each series, because of the similarity of the starting compounds, the bond cleaved and the products formed.  $E_{1,p}$  can be used for comparing reactivities as  $k_2^{\ddagger}$  is the reaction rate (eqn 2).

$$k_2^{\ddagger} = A e^{-\Delta G^\ddagger/RT} \quad (2)$$

but it relates only to the electron transfer while the reactions investigated include electrochemical and chemical steps. At the beginning of the wave, i.e. less negative potentials, the electron transfer is the slowest (eqn 3)

$$i = i_0 e^{-\alpha F \eta / RT} \quad (3)$$

and it can be rationally assumed that it is the rate determining step. We therefore chose to use  $E_{1,20}$  ( $p = 20$ ;  $i = 5\% i_0$ ) for a reactivity criterion rather than the usually accepted  $E_{1,2}$ . Applying  $E_{1,p}$  according to eqn (1), is meaningful only if the reactions are irreversible and their degree of irreversibility is identical. The slope of

$\log i / \log t$  curve of a reaction reveals whether it is irreversible and to what extent ( $i_{\text{rev}} \propto t^{1/2}$ ;  $i_{\text{irr}} \propto t^{2/3}$ ). The slopes calculated from the  $\log i / \log t$  curves (Figs. 5-7) were found to be 0.52 for 3 and 4 and 0.50 for 6 and 7 and showed almost identical irreversibility. Although a slope for 7 was not obtained (see Results) similar behavior was assumed.

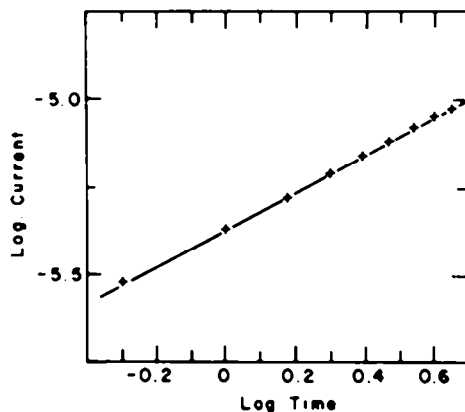


Fig. 5.  $\log i / \log t$  plot (corrected for b.g.) for  $5 \times 10^{-3}$  M phenacyl chloride 3 at  $-1.0$  V (SCE).  $0.5$  M  $\text{Et}_4\text{N-p-Ts}$  in  $\text{CH}_3\text{CN}:\text{H}_2\text{O}$  (6:1), pH 3.0.

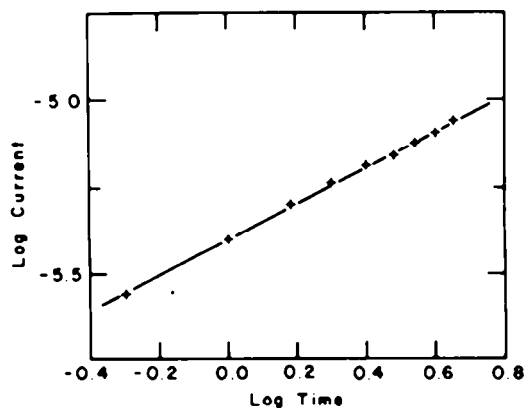


Fig. 6.  $\log i / \log t$  plot (corrected for b.g.) for  $5 \times 10^{-3}$  M phenacyl bromide 4 at  $-0.2$  V (SCE).  $0.5$  M  $\text{Et}_4\text{N-p-Ts}$  in  $\text{CH}_3\text{CN}:\text{H}_2\text{O}$  (6:1), pH 3.0.

†The potential at which the current reaches a fraction  $p$  of the limiting current:  $i_{\text{lim}} - i_0/p$ .

‡The rate of an electrochemical reaction is controlled by electron transfer or by diffusion or both. In the last case,  $E_{1,p}$  can be compared only if the electron transfer controls the reaction rates to the same extent.

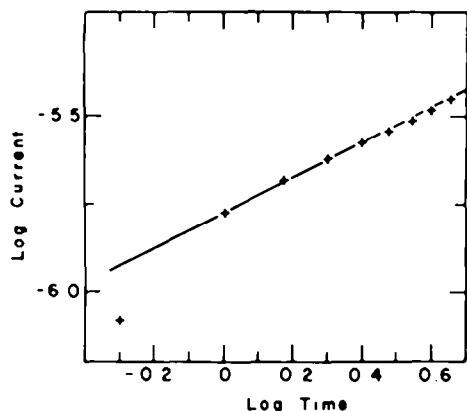
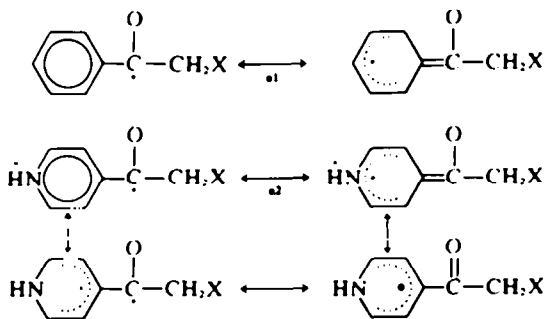


Fig. 7.  $\log i/igt$  plot (corrected for b.g.) for  $5 \times 10^{-4}$  M 4-(chloroacetyl)pyridine 6 at  $-0.2$  V (SCE).  $0.5$  M  $\text{Et}_4\text{N-p-Ts}$  in  $\text{CH}_3\text{CN}:\text{H}_2\text{O}$  (6:1), pH 3.0.

The  $E_{1/20}$  values in the table (Results) therefore seem suitable for interpretation in terms of rate limiting electron transfer. Comparison among the chlorides and bromides showed that the pyridinium derivative is much more reactive than the analogous benzene compound and this permits a distinction between mechanisms.

For a nucleophilic displacement of the halogen bond, the electrode acts as the nucleophile and the halogen leaves simultaneously with the electron attack on the carbon, the carbonyl exhibiting only the polar effect of the oxygen. The transition state in this case can be described as similar to the classical transition state for  $\text{S}_{\text{N}}2$  reactions in which there is little change of the formal charge of the participating carbon. It is not possible to rationalize the strong influence (on the reactivity of the halide) by changing a benzene by a pyridine ring, if such a transition state is assumed for reduction. However in the alternative mechanism (Scheme 2) the electron is added to the carbonyl bond (for the sake of discussion we shall assume a full electron transfer for the *trans* state). The transition state **a1** (Scheme 3) for the benzene derivatives would be stabilized by charge delocalization over the  $\pi$  electrons of the ring. More stabilization of the transition state **a2** accounting for the lower activation energy of the pyridinium derivatives is achieved by participation of the positively charged nitrogen in the electron delocalization.



Scheme 3.

It has been suggested that the "ease of reduction of these halides is generally due to formation of an especially stable radical in the initial reduction step..." This mechanism would go directly to **b** avoiding the anion radical. This mechanism is consistent with the data

presented here if there is little C-X bond breaking so that negative charge still resides on the organic fragment.

It is important to note, however, that Scheme 3 is consistent with all the literature data as well. Thus, for example, a rate limiting electron transfer to form anion radical can explain the present results extremely well. It can also explain the dependence of reduction potential on X.

The best description of the anion radical involves addition of an electron to an orbital delocalized over the carbonyl and halogen. More precisely this orbital can be visualized as resulting from mixing of the  $\pi^*$  carbonyl orbital and the  $\sigma^*$  C-X orbital. Molecules with low lying  $\sigma^*$  orbitals like  $\alpha$ -iodoketones would reduce most easily in agreement with experiment.

#### EXPERIMENTAL

**Electrodes.** A polarographic capillary served as the dropping mercury electrode. In current-potential measurements the drops were knocked off every 0.32 s by means of an electromechanical device (Metrohm, A. G. Herisau; Schweiz", E-354 polarographic stand). The maximum drop size was calculated by weighing all the drops collected in 10 min. and assuming a hemispherical shape.<sup>18</sup> In preparative experiments a mercury pool of  $15 \text{ cm}^2$  area was used as the cathode. In all experiments platinized platinum foil was used as the counter electrode and a commercial calomel (SCE) electrode ("Radiometer" K-401) served as a reference. All potentials reported in this work are vs SCE.

**Instrumentation.** The potentiostat used was "Elron, CHP-1" and it was combined with an "Elron, CHF-1" function generator for  $i/E$  measurements. Curves were obtained by means of a "Moseley 7030 AM" X-Y recorder.

**The cell.** A 5-necked flask was used (100 ml). The counter electrode was placed inside a thirsty glass ("Corning", 7930) or alundum tube (2 cm dia.) dipping into the cell. The reference electrode was enclosed in a glass tube with a Luggin capillary brought to within less than 1 mm from the working electrode. Two inlets for gas allowed passage of nitrogen through the soln or above it during the experiment.

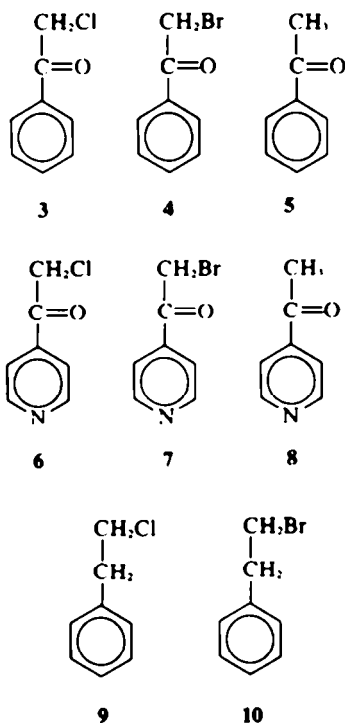
#### Electrical measurements

(a) Current-potential measurements on mercury drops of constant surface area were performed potentiostatically in the range 0 to  $-2.0$  V, varying the potential with time at a rate of 5 mV/s. Maximum currents were measured at each potential, corresponding to a maximum drop size, just before the drop was knocked off. Nitrogen was bubbled through the solution before each measurement and over it during the measurement.

Current-potential plots for different concentrations of phenacyl chloride 3, phenacyl bromide 4, acetophenone 5, 4-acetyl pyridine 8, (2-chloroethyl)benzene 9 and (2-bromoethyl)benzene 10 in b.g. (background) solution [0.5 M ethyl-*p*-toluene sulfonate ( $\text{Et}_4\text{N-p-Ts}$ ) in acetonitrile:water (6:1)] were recorded. 4-(Chloroacetyl)pyridine 6 and 4-(bromoacetyl)pyridine 7 were used as the hydrochloride and the hydrobromide, respectively (in all experiments), as they tend to polymerize when handled as free bases.<sup>19</sup> To avoid the polymerization which occurs in

Table I.  $E_{1/20}$  values for the  $\alpha$ -haloketones ( $10^{-4}$  M reactant in b.g. pH 3 solutions)

Compound	$E_{1/20}$ V (SCE)
(2-chloroethyl)benzene 9	no red. wave
phenacyl chloride 3	-0.99
4-(chloroacetyl)pyridine 6	-0.15
(2-bromoethyl)benzene 10	no red. wave
phenacyl bromide 4	-0.23
4-(bromoacetyl)pyridine 7	-0.02



acetonitrile:water solvent, their current-potential curves were measured in the b.g. solution after adjusting the pH to 3.0 by means of HCl for **6** and HBr for **7**. In order to enable meaningful comparison between the measurements for all the compounds, current-potential measurements at pH 3.0 (using both HCl and HBr in separate experiments) were performed with **3**, **4**, **5**, **8**, **9** and **10**. The halides **9** and **10** did not reduce in either b.g. or b.g. pH 3 solutions. The curves obtained for **4** in b.g. solution are shown as an example in Fig. 1.

(b) Current-time curves taken during the lifetime of a drop (on free falling drops) were performed at  $5 \times 10^{-3}$  M concentrations in b.g. solution—pH 3. The potential was constant during each measurement and was at  $E_{1.20}$  for each compound: phenacyl chloride 3-0.2 V; phenacyl bromide 4-1.0 V and 4-(chloroacetyl)pyridine 6-0.2 V. Representative curves are shown in Fig. 4 for **3**.

#### Preparative electrolysis and product analysis

All experiments were potentiostatic and were conducted on 30 ml of 0.1 M starting compound solutions. The reactions were stopped when the current dropped to b.g. value ( $\sim 5$  h). Each electrolysis was repeated several times for verification of the results and the benzene derivatives **3** and **4** yielded acetophenone **5**. The pyridine derivatives **6** and **7** yielded acetyl pyridine **8**. Both products were obtained in quantitative yield. The Faradaic yields were over 90% for **4**, **6** and **7** and 60-65% for **3**.

Electrolyses of **3** and **4** in b.g. solutions and of **3**, **4**, **6** and **7** in b.g. pH 3 solns were performed. The work up consisted of removing the acetonitrile *in vacuo* at room temp., addition of 15 ml sat. NaCl soln, extraction with ether and removing the solvent (at room temp) after drying over  $\text{MgSO}_4$ . When b.g. pH 3 solns were used KOH was added (to pH 7) prior to the ether extraction.

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